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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/845,335	05/01/2001	Barbara Clough	117-349	4115

7590 09/14/2004
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Arlington, VA 22201

EXAMINER
GRUN, JAMES LESLIE

ART UNIT PAPER NUMBER

1641

DATE MAILED: 09/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/845,335

Applicant(s)

CLOUGH ET AL.

Examiner

James L Grun

Art Unit

1641

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 November 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 17-21 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 17-21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 01 May 2001 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>01 May 2001</u> . | 6) <input type="checkbox"/> Other: _____ |

Art Unit: 1641

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Technology Center 1600, Group 1640, Art Unit 1641.

This application has been filed with informal drawings that are acceptable for examination purposes only. Applicant is required to submit acceptable corrected drawings suitable for publication within the time period set in the Office action. See 37 CFR 1.85(a). Submission of corrected drawings may no longer be held in abeyance pending the indication of allowable subject matter. Failure to take corrective action within the set period will result in **ABANDONMENT** of the application. Direct any inquiries concerning drawing review to the Drawing Review Branch at (703) 305-8404.

The disclosure is objected to because of the following informalities: page 19, line 2, -- Three-- is misspelled. Appropriate correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention, and failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

Claims 17-21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Inadequate guidance is presented for how to use the “identifying” methodology because there is nothing presented in the specification that would allow one to extrapolate from an in vitro assay system to the effect one would expect in situ (i.e. intracellularly) or in vivo. Success of any therapeutic composition is dependent not only upon a particular mode of action but also upon adequate concentrations of drug reaching the desired site of activity. For function it would seem that a compound identified by the instant method would need to possess the ability to cross the membranes of both the host cell and the parasite. The effect of a test compound on a cell extract or on an RNA fragment is not predictive of activity against intact organisms if the compound does not penetrate the membrane to arrive at the appropriate site of activity (see e.g. page 559 of Parmeggiani et al, Ann. Rev. Microbiol. 39: 557-577, 1985). It would appear that any compound “identified” by the instant method would require further unpredictable experimentation to determine if that compound functions as an anti-malarial. Thus, without such further unpredictable experimentation, experimentation which is undue, the method does not serve as “indicative that the compound is an anti-malarial” as is instantly claimed. Moreover, applicant provides no nexus believable to one of skill in the art between the ability of a compound to merely bind to the 23S rRNA encoded by *P. falciparum* plastid DNA and any ability of that compound to potentially function as an anti-malarial. Even if binding is shown to occur intracellularly between the compound and the 23S rRNA encoded by *P. falciparum* plastid DNA (see above), whether such binding has any significance in inhibiting the functioning of the

Art Unit: 1641

rRNA, and thus any anti-malarial activity, is entirely unknown and unpredictable merely by binding determination. For example, GTP or the *P. falciparum* ribosomal protein equivalent to the L11 protein of *Escherichia coli* would be expected to bind to the GTPase site of the rRNA and one would not take such binding as an indication or suggestion of anti-malarial activity of these compounds. It would therefore seem unpredictable which compounds, if any, identified with the disclosed methodology will be eventually shown to have therapeutic function. The claims are based merely on speculation that any compound identified with the in vitro screening method would be effective in vivo. For the above reasons, one would not be assured of the ability to practice the invention as instantly claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 17-21 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 17-21, “the 23S ribosomal RNA”, “the plastid DNA”, “the malaria parasite”, and “the GTPase domain” lack antecedent basis.

In claims 18 and 19, “the amount”, “the absence”, and “the presence” lack antecedent basis. The relationship of “could be an anti-malarial” to the previously claimed “is an anti-malarial” is not clear and would appear not to further limit the recitation in the independent claim.

In claims 20-21, “the position” lacks antecedent basis.

Art Unit: 1641

In claim 21, "the sequence" lacks antecedent basis.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 17, 20, and 21 are rejected under 35 U.S.C. § 102(a) as being anticipated by McConkey et al. (J. Biol. Chem. 272: 2046, Jan. 1997) in light of the known mechanism of action of the antibiotic thiostrepton as also confirmed in Rogers et al. (RNA 3: 815, August 1997).

McConkey et al. contacted the 23S ribosomal RNA (rRNA) encoded on the plastid DNA of *P. falciparum* with thiostrepton and determined growth of parasites comprising the ribosomal RNA. The reference thereby determined the binding of thiostrepton to the rRNA in light of the known mechanism of action of thiostrepton which is dependent upon binding to the GTPase domain of 23S rRNA as taught in the reference and as also confirmed in Rogers et al.

Claims 17, 20, and 21 are rejected under 35 U.S.C. § 102(a) as being clearly anticipated by Rogers et al. (RNA 3: 815, August 1997).

Rogers et al. contacted a fragment of the 23S ribosomal RNA (rRNA) encoded on the plastid DNA of *P. falciparum* corresponding to the nucleotide 1051-1109 GTPase domain in the 23S rRNA of *E. coli* with thiostrepton and determined binding thereto (see e.g. Fig. 2).

Art Unit: 1641

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Donovick et al (U.S. Patent No. 2,982,689) teach thiostrepton.

Garrett (TIBS 8: 189, 1983) teaches the binding of thiostrepton to 23S rRNA.

Beckers et al. (J. Clin Invest. 95: 367, 1995) propose the ribosomes encoded on the plastid DNA of Apicomplexan parasites as antimicrobial targets.

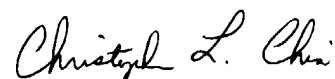
Any inquiry concerning this communication or earlier communications from the examiner should be directed to James L. Grun, Ph.D., whose telephone number is (571) 272-0821. The examiner can normally be reached on weekdays from 9 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, SPE, can be contacted at (571) 272-0823.

The phone numbers for official facsimile transmitted communications to TC 1600, Group 1640, are (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application, or requests to supply missing elements from Office communications, should be directed to the Group receptionist whose telephone number is (571) 272-1600.

James L. Grun, Ph.D.
September 8, 2004



CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP 1800-1641

9/10/04